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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,376	09/10/2003	Dan Nilsson	NILSSON=6B	5425
1444	7590	06/01/2005	EXAMINER	
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			AFREMOVA, VERA	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/658,376

Applicant(s)

NILSSON, DAN

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-5, 12-26, 28 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-11 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5/02/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of the Group II (claims 6-11 and 27) in the reply filed on 5/02/2005 is acknowledged. The traversal is on the ground(s) that the group I claims, drawn to a product, are allowable and, thus, the process claims should be rejoined. This is not found persuasive because patentability of instant claims 6-11 and 27 is not established. Further, the process claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. MPEP 821.04. Therefore, the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1-5, 12-26, 28 and 29 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 5/02/3005.

Claims 6-11 and 27 are under examination in the instant office action.

Claim Rejections - 35 USC § 112***Deposit***

Claim 11 is rejected under 35 U.S.C. 112, *first paragraph*, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At least some of the claims require one of ordinary skill in the art to have access to a specific strains *Lactococcus lactis subsp. lactis* DN221 (DSM 11034) and *Lactococcus lactis subsp. lactis* DN227 (DSM 11040). Because the microorganisms are essential to the claimed

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invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganisms are not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by deposit of the microorganism. The specification does not disclose a repeatable process to obtain the claimed specific strains because the selection method involves unpredictable effects of mutagenesis on parent culture(s). It is not particularly clear from the specification or record that the strains are readily available to the public.

The rejection may be overcome by establishing that each microorganism identified is readily available to the public and will continue to be so for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, or by an acceptable deposit as set forth herein. See 37 CFR 1.801-1.809.

If the deposit of strains *Lactococcus lactis subsp. lactis* DN221 (DSM 11034) and *Lactococcus lactis subsp. lactis* DN227 (DSM 11040) is made under the terms of the Budapest Treaty then an affidavit or declaration by applicants or a statement by an attorney of record over his/her signature and registration number, stating that the deposit has been made under the Budapest Treaty and that all restrictions imposed by the depositor on availability to the public of the deposited material will be irrevocably removed upon issuance of the patent would satisfy the deposit requirement. See 37 CFR 1.808.

Because DSM has acquired the status of an International Depository in accordance to the Budapest Treaty, a declaration stating that all restrictions will be irrevocably removed upon issuance of the patent will overcome this rejection.

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Indefinite

Claims 6-11 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 7 are rendered indefinite by relative comparison of the claimed bacterium to its generic parent (wild-type) strain. The terms such as “essentially the same” “reduced” and/or “increased” rates of bacterial growth and/or various metabolite productions are not defined by the claim. The specification does not provide a standard for ascertaining the requisite degree. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Components of M17 and RSM media are not clearly point out and thus, the criticality of claimed features including grow or metabolite production on these media for the claimed bacterium and for the generic parent strains are uncertain.

Claim 6 is rendered indefinite by recitation of steps of the method of making claimed bacterium because selection conditions and active steps are unclear as claimed. It is uncertain what is the meaning of “providing” and what is the source of wild-type lactic bacteria. It is uncertain what are “said conditions” in the selecting steps. It is uncertain what are the differences between “providing” and “selecting” steps because both appear relate to selection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 7 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Mat-Jan et al. (IDS reference; Journal of Bacteriology. 1989, Vol.171, No. 1, pages 342-348) in the light of evidence by Hugenholtz (IDS reference; FEMS Microbiology Reviews 1993, 12, 165-178).

Claims are directed to a PFL defective lactic acid bacterium or to the lactic bacterium mutant that is lacking enzyme PFL (pyruvate formate lyase). The claimed bacterium is characterized relatively to the parent or wild-type strain by at least one characteristics such as that it does not produce formate under anaerobic conditions, does not produce ethanol under anaerobic conditions, is characterized by production of acetolactate-derived metabolite(s), is characterized by capability to grow on M17 medium under aerobic conditions and has reduced growth on M17 medium under anaerobic conditions. The claimed bacterium is made by selection of mutants that does not growth on acetate-containing medium under anaerobic conditions. Some claims are further drawn to production of acetoin. Some claims are further drawn to a starter composition comprising the PFL defective lactic acid bacterium.

Mat-Jan et al discloses lactic bacterium mutants of *E.coli* that are lacking enzyme PFL (see abstract). *E.coli* is a lactic bacterium within the meaning of the claims because it produces lactic acid (page 346, col. 2, par. 3, lines 5-8). The disclosed mutants of *E.coli* can grow as the parent strain(s) on the same basic media including at least some components of M17 or RSM. Due to the lack of deficiency of PFL the lactic bacteria including *E.coli* do not produce formate, ethanol and acetate and they are reasonably expected to produce more of acetolactate-derived metabolite(s) including acetoin by alternative enzymatic pathway (See Fig. 1, page 168, of the reference by Hugenholtz that is cited below). The pfl defective mutants of *E.coli* cannot growth

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anaerobically on glucose minimal medium (in the absence of acetate) but addition of acetate allows them to grow by lactate fermentation (page 342, col.1, last par.). Thus, the PFL defective mutants of *E.coli* are provided or selected by the same method of making. The PFL defective mutant of *E.coli* in a culture medium is a starter composition within the meaning of the claims. Thus, the cited reference anticipates the claimed PFL defective lactic bacterium.

Claims 6-10 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Hugenholtz (IDS reference; "Citrate metabolism in lactic bacteria". FEMS Microbiology Reviews 1993, 12, 165-178) or by Starrenburg et al. ("Citrate fermentation by *Lactococcus* and *Leuconostoc spp.*" Applied and Environmental Microbiology. December, 1991. Vol. 57, No. 12, pages 3535-3540) in the light of evidence by ATCC Catalogue.

Claims 6, 7 and 27 as explained above. Claims 8-10 are further drawn to lactic bacterium belonging to the species of *Leuconostoc*, *Lactobacillus*, *Streptococcus*, *Bifidobacterium*, *Pediococcus*, *Lactococcus* including *Lactococcus lactis subsp. lactis/diacetalicus*.

The reference by Hugenholtz discloses a PFL defective lactic acid bacterium or the lactic bacterium mutants belonging to *Leuconostoc* species that are lacking enzyme PFL (page 171, col.2, par. 3, lines 5-8). In view of the Fig. 1 teaching, the PFL lacking mutant does not produce formate, acetate and ethanol and it is characterized by production of acetolactate-derived metabolite(s) including acetoin as required for the claimed bacterium. The PFL defective mutant in a culture medium is a starter composition within the meaning of the claims

The reference by Starrenburg et al. discloses a PFL defective lactic acid bacterium belonging to *Leuconostoc* species or "*Leuconostoc* 60" that does not produce formate under

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anaerobic conditions (table 1, page 3537), does not produce ethanol but produces acetolactate-derived metabolite(s) including acetoin and butanediol. The PFL defective mutant in a culture medium is a starter composition within the meaning of the claims

Although characteristics of the parent or wild type strains of the referenced PFL mutants are not indicated or disclosed, the relative enhancement and/or relative differences of claimed features cannot be determined and they would not be meaningful unless some specific and particular strains are claimed.

Although it is uncertain how the referenced bacteria have not been made, provided or selected, they are the pfl defective mutants and, thus, they are characterized by the same features that are required during selection method that is encompassed by the claims.

Although the referenced bacteria are characterized as belonging to *Leuconostoc*, the lactic bacteria belonging to *Leuconostoc*, *Lactobacillus*, *Streptococcus*, *Bifidobacterium*, *Pediococcus*, *Lactococcus* including *Lactococcus lactic subsp. lactis/diacetalicus* have been frequently cross-identified and reclassified between these genera and species (as demonstrated by ATCC catalogue, see pages 68, 199, 205, 264 and 346) and, thus, there is a reasonable believe that the pfl defective lactic bacteria of the cited references might be assigned to any and all of the presently claimed genera and/or species.

With respect to claims 11 it is noted that deposit requirement has not been met for DSM 11304 and DSM 11040. With regard to the claimed DSM 11034 (DN221) it is noted that it has been selected by the claimed method (page 25) and is shown as essentially lacking production of formate (page 26, lines 19-22; page 33, table 4.3). However, there is no any disclosure with

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regard to the final properties of the claimed DSM 11040 (DN227) particularly as related to pfl deficiency including essentially no formate production as encompassed by claim 6 for the specific strains of claim 11.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

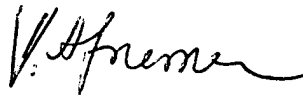
The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

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May 26, 2005

A handwritten signature in black ink, appearing to read 'V. Afremova', with a stylized, flowing script.

VERA AFREMOVA

PRIMARY EXAMINER